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| EXAMINER | |
|---|---|
| LU,F | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1655 | 10 |

DATE MAILED: 06/08/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/204,865 | Applicant(s) Chen et al., |
|---|---|---|
| | Examiner Frank Lu | Group Art Unit 1655 |

☒ Responsive to communication(s) filed on *Mar 16, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claim**

☒ Claim(s) *1-11, 13-15, 21-36, 40, 41, 44, 50-52, and 57-67* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11, 13-15, 21-36, 40, 41, 44, 50-52, and 57-67* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *9*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

## DETAILED ACTION

### *Restriction/Election*

1. Applicant's election without traverse of claims 1-36, 40, 41, 44, and 50-56 is acknowledged. The restriction is made final.

### *Specification*

2. Upon review of applicants' amendments and remarks, the objection on the specification in the first office action has been withdrawn by the examiner.

### *Drawings*

3. The drawings remain objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

### *Claim Objections*

4. Upon review of applicants' amendments and remarks, the claim objections in the first office action has been withdrawn by the examiner.

***Claim Rejections - 35 USC § 112***

5. Upon review of applicants' amendments and remarks, the rejection in the first office action under 35 U. S. C 112, second paragraph (indefinite) has been withdrawn by the examiner.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-11, 13-15, 21-36, 40, 41, 44, 50, 51, and 57-65 are rejected under 35 U.S.C. 112, first paragraph, while the specification contains subject matter which described the immobilization of 3' -aminated oligonucleotides onto a three-dimensional porous substrate but the specification does not contain subject matter which was not described the immobilization of any kind and any length of polynucleotides onto a three-dimensional porous substrate in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is note that the specification only provides an adequate written description of the immobilizing 3' -aminated oligonucleotides onto a three-dimensional porous substrate (see specification, pages 37-44). However, the specification does not provides an adequate written description of immobilizing any kind and any length of polynucleotides onto a three-dimensional porous substrate.

It is note that the specification does not provide an adequate written description to show how to yield an activated surface area with about $6 \times 10^{-17}$ and $9 \times 10^{-15}$ nmol/nm$^2$ reactive groups on a three-dimensional porous substrate as described in claim 65.

It is note that the specification does not provide an adequate written description to show how to covalently attach a capture polynucleotide to the porous substrate via a phosphodiester, phosphorothioate or phosphoramidate linkage as described in claims 6, 30, 57, and 61.

In order for the skilled artisan to practice the full scope of the invention, sd. skilled artisan would have to resort to undue experimentation, these experiments can not be performed with the guidance provided by the application.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. The term "high density or high molecular weight" in claims 10, 34, and 67 is a relative term which renders the claim indefinite. The term "high density or high molecular weight" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

9. The term "high stringency or low stringency or moderate stringency" in claims 24, 25 and 36 is a relative term which renders the claim indefinite. The term "high stringency or low stringency or moderate stringency" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

*Claim Rejections - 35 USC § 102*

10. Upon review of applicants' amendments and remarks, the rejection in the first office action under 35 U. S. C 102 has been withdrawn by the examiner.

*Claim Rejections - 35 USC § 103*

11. Upon review of applicants' amendments and remarks, the rejection in the first office action under 35 U. S. C 103 (a) has been withdrawn by the examiner.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-5, 8-11, 13-15, 21-29, 32-36, 40, 41, 44, 50-52, 58-60, 62-64, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness *et al.*, (European Patent 0455,905A2, issued on November 13, 1991) in view of Fahy *et al.*, (Nucl. Acid Res, 21, 1819-

1826, 1993) and in view of Chamberland (Canadian Patent 1,110,511, issued on November 13, 1981).

Van Ness *et al.* teach the solid supports for nucleic acid hybridization assay. The capture oligonucleotides first were modified at either the 5' or 3' end with a space arm containing a blocked amine group (page 5, the third and fourth paragraphs). After activation, they were covalently linked onto NytranTM membrane and nylon beads treated with alkylating agents. The bead could be employed free in solution, in a flow-through format such as in a column or a dipstick (Page 2, the tenth paragraph). Target oligonucleotide was biotinylated and could be detected by peroxidase-HRP substrate system after the hybridization (page 12, 4 and 5 paragraphs).

Van Ness *et al.* do not disclose a flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate and calculation of the quantities of capture oligonucleotide in the flow-through device.

Fahy *et al.* teach that bromoacetyl and thiol oligonucleotide derivative covalently link onto sulfhydryl- and bromoacetyl-polyacrylamide support (Biogel and Trisacryl resins). The end-attachment efficiencies for the oligoucleotides is greater than 95%. Note that Bio-Gel beads used in this publication are spherical in shape with a diameter ranging from 45 to 180 μm (see Bi-Rad Catalog, 1998/99). Thus we can reasonably approximate pores between beads in a column format to be the size of a bead equal to the diameter of the bead even through no exact porous size is available.

Fahy *et al.* do not teach to hybridization using a flow-through device.

Chamberland teach an unidirectional fluid membrane. The membrane is in the form of a sheet of porous plastic material comprising a multitude of interconnected pores that together define passages suitable to allow a gas such as air to flow (abstract). The membrane which is in the form of a sheet of porous plastic material can be made of polypropylene or polyethylene (page 6, lines 25-28) with thickness ranging from about 1/16 to ½ inch and a interconnected pore size ranging from 8 to 250 $\mu$m. Since this membrane fits the thickness and pore size of the claimed three-dimensional porous substrate, we can reasonable consider that said porous substrate has a void volume in the range of about 1 $\mu$l/cm$^2$ to about 100 $\mu$l/cm$^2$ and a porosity in the range of about 25%-80%.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have immobilized a capture polynucleotide onto a flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate, have tested different hybridization conditions as needed (high, moderate and low stringencies as in claims 24, 25, and 36, hybridization time as claim 26), and have calculate how many captured polynucleotides to attach on a porous substrate (ie. instant claim 4) to decrease and/or increase oligonucleotide end-attachment efficiency suggested by Fahy *et al.* as needed for various sample amounts. The patent published by Chamberland would have motivated one having ordinary skill in the art to test whether flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate could be used to immobilize a capture polynucleotide as suggested by Van Ness *et al.* and finding proper conditions to perform the flow-through hybridization assay (page 1826, the column 1, the second paragraph). One having ordinary skill in the art at the time

the invention was made would have been a reasonable expectation of success to combine these methods together because all of these methods are known in the art and are easy to use.

14. Claims 1-3, 8-11, 13-15, 21-27, 29, 32-36, 40, 41, 44, 50-52, 58-60, 62-64, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feindt *et al.*, (European Patent 0605,828A1, July 13, 1994) in view of Chamberland (Canadian Patent 1,110,511, issued on November 13, 1981).

Feindt *et al.* teach flow-through hybridization assay for oligonucleotides. In this method, different amount of capture DNA were spotted onto Biodyne B membrane (0.2 or 0.45 or 1.2 μm from Pall Biosupport Corporation) and wet with NaOH. This flow-through assay device includes Pall Biodyne B membrane, polycarbonate layer, polyester layer and absorbent layer as shown in Figure 1. The capture DNAs were crosslinked onto the membrane with UV (page 6, line 9-14 and table). The biotinylated target DNA was flowed through the device and finally detected by anti-biotin conjugated liposomes containing sulforhodamine B dye (page 6. the fourth paragraph). Note that flow-through membrane hybridization assay requires no period of incubation of the sample with the membrane (page 3, the fourth paragraph).

Feindt *et al.* do not disclose a flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate.

The teachings of Chamberland has been summarized previously, *supra.*

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have immobilized a capture polynucleotide onto a flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate and have tested

different hybridization conditions as needed (high, moderate and low stringencies as in claims 24, 25, and 36, hybridization time as claim 26). The patent published by Chamberland would have motivated one having ordinary skill in the art to test whether flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate could be used to immobilize a capture polynucleotide as suggested by Feindt *et al.* and finding proper conditions to perform the flow-through hybridization assay. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these methods together because all of these methods are known in the art and are easy to use.

15. Claims 1-3, 5, 7-11, 13-15, 21-27, 29, 31-36, 40, 41, 44, 50-52, 58-60, 62-64, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tam (US Patent 5,741,647, filed on Feb. 16, 1996) in view of Chamberland (Canadian Patent 1,110,511, issued on November 13, 1981).

Tam teaches the determination of a target nucleic acid present in a sample using flow through hybridization device. This device is a multiple-well plate which consists of two stainless plates, two gaskets, one blotting membrane and one temperature regulated controlled block as shown in Figure 1. In this method, the a large number of capture oligonucleotide (20-24 nt), used to capture the target DNA molecules, are covalently immobilized onto the Biodyne C membrane (page 2, line 1-4). Note that the porous substrate used is Biodyne C membrane with porosity about 0.45 micron (page 2, the second paragraph, line 4) and $HN_2$-$(CH_2)_3$-moiety on 5' end of a capture oligonucleotides reacts with -COOH group on 3' end of Biodyne C membrane and forms a covalently carboxyamide linkage (page 12, example IV, line 6-10). Target DNA was amplified

by PCR using biotin-11-dUTP and dNTP and was flowed through the device. The hybridization conditions may vary dependent on the experimental conditions. After final washing, the signal could be developed by the incubation with streptavidin-HRP conjugate (page 10, example 1).

Tam does not disclose a flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate.

The teachings of Chamberland has been summarized previously, *supra.*

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have immobilized a capture polynucleotide onto a flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate and have tested different hybridization conditions as needed (high, moderate and low stringencies as in claims 24, 25, and 36, hybridization time as claim 26). The patent published by Chamberland would have motivated one having ordinary skill in the art to test whether flow-through device comprising a about 1 mm to 20 mm thick three-dimensional porous substrate could be used to immobilize a capture polynucleotide as suggested by Tam and finding proper conditions to perform the flow-through hybridization assay. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these methods together because all of these methods are known in the art and are easy to use.

***Conclusion***

16. Rejections found in the prior office action yet not restated herein above have been withdrawn.

17. No claim is allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
June 2, 2000

B. L. Sisson

BRADLEY L. SISSON
PRIMARY EXAMINER
GROUP 1800